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36 and 47 have been amended. Support for the amendments and new claims can be found throughout the specification and in the claims as filed. In particular, support for the amendment to claims 12, 23, 36 and 47 can be found, for example, on page 39, line 24, to page 40, line 18. Claim 13 has been amended to incorporate dependent claim 17. Support for new claims 48-51 and 52-55 can be found in original claims 23 and 36, respectively. Support for new claims 56-70 can be found in original claims 1-12. Accordingly, these amendments and new claims do not raise an issue of new matter and entry thereof is respectfully requested.

Applicant has set forth the amendment to the claims in clean form above and in Appendix A, with marked up amendments indicated with brackets and underlining.

Applicant appreciates the time and helpful discussion with Examiner Mahatan and Examiner Allen in the telephone interview with Applicant and Applicant's representative on March 25, 2003. Applicant also appreciates the Examiner's consideration of comments made during the telephone interview regarding enablement and the prior art references and indication in the interview and Interview Summary that agreement was reached on certain issues. It is believed that the comments below address the issues discussed in the telephone interview.

Applicant also appreciates the Examiner's indication that all of the species are being examined.

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Rejection Under 35 U.S.C. § 112, First Paragraph

The rejection of claims 2, 4, 5, 14-16, 24-35, and 37-46 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully traversed. As discussed in the telephone interview, the specification teaches that a "characteristic" used in reference to a polypeptide refers to a physicochemical property of a polypeptide (page 16, lines 5-27). The Office Action acknowledges that the specification is enabling for physicochemical properties. Applicant appreciates the Examiner's consideration of comments regarding support for the enablement of the claims and indication that the enablement rejection would be withdrawn in view of the description on page 16. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 102

The rejection of claims 1, 2, 4-10, 12, 24, 25, 27-31, 33-38, 40-42, and 44-47 under 35 U.S.C. § 102(a) as allegedly anticipated by Masselon et al., Anal. Chem. 72:1918-1924 (2000), is respectfully traversed. Applicant respectfully submits that these claims are novel over Masselon et al.

Applicant appreciates the Examiner's consideration of comments about Masselon et al. made during the telephone interview. As discussed in the telephone interview, Figure 2B provides an exemplary illustration of an embodiment of mass spectrometry determination in the absence of ion selection, which

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is described, for example, on page 5, lines 11-22; page 14, lines 23-30; page 15, line 27, to page 16, line 4; page 26, lines 19-30; and page 55, lines 18-28. Applicant also appreciates the indication in the interview and Interview Summary that agreement was reached that Masselon et al. does not teach the claimed invention with respect to absence of ion selection. For the Examiner's convenience, it is pointed out that independent claims 13 and 24 and new claim 56 recite the phrase "in the absence of ion selection."

Regarding claim 1, Applicant respectfully submits that Masselon et al. does not teach the claimed method using an annotated polypeptide index. The specification teaches that an annotated polypeptide index refers to an index comprising at least one empirically determined characteristic for each of the polypeptides in the index (page 19, line 28, to page 20, line 8).

The specification also teaches that a characteristic can be determined empirically or can be predicted based on known information about the polypeptide such as sequence information (page 16, lines 20-23). The specification further teaches that a polypeptide identification index can be based on deduced characteristics of a polypeptide, for example, a characteristic deduced from genetic sequence databases, or can be determined empirically as with an annotated polypeptide index (page 27, lines 19-24). Thus, the specification teaches that an annotated polypeptide index has at least one empirically determined characteristic and is an alternative to a polypeptide identification index based on deduced characteristics of a sequence database.

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In contrast, Masselon et al. does not teach a method using an annotated polypeptide index. In particular, Masselon et al. describes using a database consisting of "predicted proteins initially reported for the full *Caenorhabditis elegans* genome sequence" (emphasis added) (page 1919, second column, last 3 lines). This reference is clearly describing the use of databases based on predicted values, not the annotated polypeptide index comprising at least one empirically determined characteristic, as in the claimed methods.

Regarding claim 37, Masselon et al. does not teach a method where the fragment mass is determined by mass spectrometry at an accuracy in ppm of greater than 2.5 ppm. Furthermore, Masselon et al. does not teach methods using the lower mass accuracies (higher ppm) recited in claims 41-43.

Applicant submits that the claimed methods are novel over Masselon et al. Accordingly, it is respectfully requested that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 103

The rejection of claims 1-10, 12-21, 23-31, 33-42, and 44-47 under 35 U.S.C. § 103 as allegedly obvious over Masselon et al., *supra*, in view of Gygi et al., Nature Biotechnol. 17:994-999 (1999), is respectfully traversed. Applicant submits that the claims are unobvious over Masselon et al., alone or in combination with Gygi et al.

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As discussed above, Masselon et al. does not teach or suggest the claimed methods. Furthermore, Gygi et al. cannot cure the deficiencies of Masselon et al. Accordingly, the claimed methods are unobvious over Masselon et al., alone or in combination with Gygi et al., and Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 1-47 under 35 U.S.C. § 103 as allegedly obvious over Masselon et al., *supra*, in view of Gygi et al., *supra*, and further in view of Easterling et al., Anal. Chem. 71:624-632 (1999), is respectfully traversed. Applicant submits that the claims are unobvious over Masselon et al., alone or in combination with Gygi et al. and further in view of Easterling et al.

~~As discussed above, Masselon et al. does not teach or~~
suggest the claimed methods. Furthermore, neither of Gygi et al. or Easterling et al., alone or in combination, can cure the deficiencies of Masselon et al. Accordingly, the claimed methods are unobvious over Masselon et al., alone or in combination with Gygi et al. and/or Easterling et al., and Applicant respectfully requests that this rejection be withdrawn.

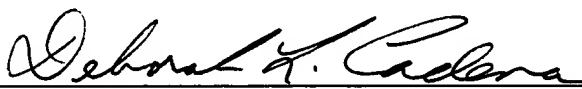
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CONCLUSION

In light of the amendments and remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. The Examiner is invited to call the undersigned agent or Cathryn Campbell if there are any questions.

Respectfully submitted,

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APPENDIX A

12 (Twice amended) The method of claim 2, wherein said characteristics are selected from the group consisting of polypeptide mass, amino acid composition, isoelectric point (pI), and **[order of]** elution on a chromatographic medium.

13. (Amended) A method for identifying a polypeptide, comprising:

(a) simultaneously determining the mass of a subset of parent polypeptides from a population of polypeptides and the mass of fragments of said subset of parent polypeptides, wherein said fragment mass is determined by mass spectrometry in the absence of ion selection for producing fragment ions;

(b) comparing said determined masses to an annotated polypeptide index;

(c) identifying one or more polypeptides of said annotated polypeptide index having said determined masses; and

(d) quantitating the amount of said identified polypeptide in a sample containing said polypeptide.

23. (Amended) The method of claim 13, wherein said characteristics are selected from the group consisting of polypeptide mass, amino acid composition, isoelectric point (pI), and **[order of]** elution on a chromatographic medium.

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36. (Amended) The method of claim 24, wherein said characteristics are selected from the group consisting of polypeptide mass, amino acid composition, isoelectric point (pI), and **[order of]** elution on a chromatographic medium.

47. (Amended) The method of claim 37, wherein said characteristics are selected from the group consisting of polypeptide mass, amino acid composition, isoelectric point (pI), and **[order of]** elution on a chromatographic medium.
